REMARKS

Claims 1, 4, 8, 37, 40 and 55-58 are pending in the subject application. By this Amendment, applicants have cancelled claims 37, 40, 56 and 58, and amended claims 1, 8, 55 and 57. Accordingly, claims 1, 4, 8, 55 and 57 are now pending in the subject application.

A marked up version of the amended claims is attached hereto as **Exhibit A**, pursuant to the requirements of 37 C.F.R. §1.121.

In view of the amendments and arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1, 4, 8, 37, 40 and 55-58 for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Specifically, the Examiner alleged that the language "relates to susceptibility" is vague and indefinite because the nature of the relationship is not defined.

In response to the rejection of claims 37, 40, 56 and 58, applicants note that these claims have been cancelled, making the rejection thereof moot.

In response to the rejection of claims 1, 4, 8, 55 and 57, applicants note that these claims do not recite the language "relates to susceptibility", rendering moot the basis for the

rejection.

In view of the above remarks, applicants maintain that claims 1, 4, 8, 55 and 57 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Claim Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 1, 4, 8, 37, 40 and 55-58 under 35 U.S.C. §103(a), alleging that the claims are obvious over Capon et al. in view of Lu et al. and Wang et al.

In response to the Examiner's rejection of claims 37, 40, 56 and 58, applicants point out that these claims have been cancelled, rendering the rejection thereof moot.

In response to the rejection of claims 1, 4, 8, 55 and 57, applicants respectfully traverse, and maintain that the Examiner has failed to establish a *prima facie* case of obviousness.

Briefly, claims 1, 4 and 8 provide a method for detecting the susceptibility of hepatitis C viral replication to an anti-hepatitis C virus drug. This method comprises, in relevant part, the use of a patient-derived hepatitis C viral gene-containing segment incorporated into a test vector, and a comparative measurement of indicator gene expression so as to permit determining drug susceptibility. Claims 55 and 57 depend from claim 1 and provide methods for detecting anti-hepatitis C virus drug resistance in a patient.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the cited references, when combined, teach or suggest every element

of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that the cited references fail to support a *prima facie* case of obviousness of the rejected claims.

First, applicants note that Capon et al. is not prior art with respect to the subject application under 35 U.S.C. §103(c) and M.P.E.P. 706.02(l)(1). Specifically, under 35 U.S.C. §103(c), "[s]ubject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person." Applicants note that the subject matter of Capon et al. and the claimed invention were, at the time the subject invention was made, owned by, or subject to an obligation of assignment to, ViroLogic, Inc., the assignee of record. In support of this statement, applicants annex hereto as **Exhibit B** a Statement Under M.P.E.P. 706.02(l)(2)(II). Accordingly, applicants maintain that Capon et al. is not prior art against this application.

Second, for the remaining references Lu et al. and Wang et al., these references, when combined, fail to teach each and every element of the claimed methods. For example, Lu et al. and Wang et al. fail to teach the use of a hepatitis C test vector-containing cell to obtain anti-hepatitis C drug susceptibility information. Likewise, these two references fail to provide a motive to combine such elements or a reasonable expectation of

success. For this reason, applicants maintain that the rejected claims are not *prima facie* obvious over Capon et al. in view of Lu et al. and Wang et al.

In view of the above remarks, applicants maintain that claims 1, 4, 8, 55 and 57 satisfy the requirements of 35 U.S.C. §103(a).

Obviousness-Type Double Patenting

The Examiner rejected claims 1, 4, 8, 37, 40 and 55-58 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable either over claims 1, 4, 7-11, 13, 14, 46-49, 51-53, 70-73 and 78-83 of U.S. Patent No. 5,837,464 (the '464 patent) in view of Lu et al. and Wang et al. or over claims 1, 2, 18, 24-27, 30-42 of U.S. Patent No. 6,242,187 (the '187 patent) in view of Lu et al. and Wang et al.

In response to the Examiner's rejection of claims 37, 40, 56 and 58, applicants point out that these claims have been cancelled, rendering the rejection thereof moot.

In response to the rejection of claims 1, 4, 8, 55 and 57, applicants respectfully traverse the Examiner's rejection, maintaining that the Examiner has failed to establish a *prima facie* case of obviousness.

Claims 1, 4, 8, 55 and 57, Lu et al., Wang et al., and the standard for establishing *prima facie* obviousness are set forth above.

Applicants maintain that neither the '464 patent nor the '187 patent, in combination with Lu et al. and Wang et al., teach each

and every element of the claimed methods, e.g., the use of a hepatitis C test vector-containing cell to obtain anti-hepatitis C drug susceptibility information. Likewise, these combinations of references fail to provide a motive to combine such elements or a reasonable expectation of success. For this reason, applicants maintain that the rejected claims are not *prima facie* obvious over either the '187 patent or the '464 patent in view of Lu et al. and Wang et al.

In view of the above remarks, applicants maintain that claims 1, 4, 8, 55 and 57 are not obvious over claims 1, 4, 7-11, 13, 14, 46-49, 51-53, 70-73 and 78-83 of the '464 patent or claims 1, 2, 18, 24-27, 30-42 of the '187 patent, each in view of Lu et al. and Wang et al.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection and earnestly solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $460.00 for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231.

7/29/02

Alan J. Morrison Date
Reg. No. 37,399

Applicants: Daniel J. Capon et al.
Serial No.: 09/126,559
Filed: June 30, 1998

MARKED UP VERSION OF THE AMENDED CLAIMS

1. (2X Amended) A method for determining the susceptibility of hepatitis C viral replication to an anti-hepatitis C virus (HCV) drug comprising:

(a) [introducing a resistance test vector comprising a patient-derived segment which comprises a hepatitis C virus (HCV) gene and an indicator gene into a host cell] culturing a host cell in the presence of the anti-hepatitis C virus drug, wherein the host cell has introduced thereto a resistance test vector comprising (i) a patient-derived segment comprising a hepatitis C virus gene and (ii) an indicator gene, wherein the expression of the indicator gene is dependent upon the patient- derived segment;

(b) [culturing the host cell from (a)] measuring the expression of the indicator gene in the host cell from step (a); and

(c) [measuring expression of the indicator gene in a target host cell, wherein the expression of the indicator gene is dependent upon the patient-derived segment;] comparing the expression of the indicator gene as measured in step (b) with the expression of the indicator gene measured in the host cell of step (a) cultured in the absence of the anti-hepatitis C virus drug, whereby greater expression of the indicator gene measured in step (c) relative to that measured in step (b) indicates susceptibility of hepatitis C viral replication to the anti-hepatitis C virus drug.

[(d) comparing the expression of the indicator gene from (c) with the expression of the indicator gene measured when steps (a) - (c) are carried

out in the absence of the anti-HCV drug,

wherein a test concentration of the anti-HCV drug is present at steps (a) - (c); at steps (b) - (c); or at step (c) and a change in expression of the indicator gene in (c), as compared to (d), relates to susceptibility of HCV replication to the anti-HCV drug.]

8. (Amended) The method of claim [5] 1, wherein [the functional viral sequence comprises an IRES] the patient-derived segment comprises a viral sequence comprises an internal ribosome entry site.

55. (2X Amended) A method for determining [resistence of hepatitis C virus (HCV) to an anti-HCV drug in a patient comprising] anti-hepatitis C virus drug resistance in a patient comprising:

(a) developing a standard curve of drug susceptibility for [such anti-HCV drug] an anti-hepatitis C virus drug;

(b) determining the susceptibility [of HCV replication to such anti-HCV drug in the patient according to the method of claim 1] to the anti-hepatitis C virus drug in the patient according to the method of claim 1; and

(c) comparing the [anti-HCV drug susceptibility from step (b) with the standard curve from step (a), wherein a decrease in susceptibility of HCV replication to the anti-HCV drug indicates development of resistance to the anti-HCV drug in the patient] anti-hepatitis C virus drug susceptibility determined in step (b) with the standard curve of step (a), whereby anti-hepatitis C drug susceptibility which is decreased relative to that shown by the standard curve indicates anti-hepatitis C drug resistance in the patient.

57. (2X Amended) A method for determining [resistance of hepatitis C virus (HCV) to an anti-HCV drug] anti-hepatitis C virus drug resistance in a patient comprising:

(a) determining [susceptibility of hepatitis C viral replication in the patient to the anti-HCV drug at a first time according to the method of claim 1, wherein the patient-derived segment is obtained from the patient at about said time] in the patient the susceptibility to an anti-hepatitis C virus drug at a first time point according to the method of claim 1, wherein the patient-derived segment is obtained from the patient at about the same time as the first time point;

(b) determining [susceptibility of hepatitis C viral replication of the same patient to the anti-HCV drug at a later time] in the patient the susceptibility to the anti-hepatitis C virus drug at a second time point; and

(c) comparing [the anti-HCV drug susceptibilities from steps (a) and (b), wherein a decrease in susceptibility of HCV replication to the anti-HCV drug at the later time as compared to the first time indicates development or progression of resistance to the anti-HCV drug in the patient] the anti-hepatitis C virus drug susceptibilities determined in steps (a) and (b), wherein a decrease in anti-hepatitis C drug susceptibility at the second time point relative to that of the first time point indicates anti-hepatitis C virus drug resistance in the patient.